

REMARKS

Applicants respectfully request reconsideration of the present application in view of the following commentary.

I. Introduction

No claim amendments are made in this response. Claims 1-41 and 43-108 are pending, with claims 8, 15-16, 23-27 and 48-108 withdrawn from consideration.

Applicants respectfully request the Examiner to clarify whether the rejection under 35 U.S.C. §102(b) has been withdrawn.

In the Office Action dated August 28, 2007, the Examiner rejected claims 1-5, 7 and 9-13 under 35 U.S.C. §102(b) for alleged anticipation by Krause *et al.*, *International Journal of Pharmaceutics*, 27: 145-155, 1985 (“Krause”). Applicants filed a response on November 26, 2008 and responded to the rejection.

In both the Office Action dated March 18, 2008 and the final Office Action dated September 16, 2008, the Examiner commented that “Applicant’s arguments against 102(b) rejection...[are] not found persuasive” (page 2, last paragraph, and page 3, first paragraph, respectively).

Because the Examiner explicitly states in the outstanding final Office Action that “the rejection was made under 35 U.S.C. § 103(a) and not found anticipatory” (page 3, lines 3-4) and that “the claims were rejected under 103(a) and not under 102” (page 4, lines 3-4), Applicants presume that the rejection under 35 U.S.C. § 102(b) has been withdrawn.

II. Provisional Double Patenting Rejection

Claims 1, 4-7, 9-12, 14, 18-21 and 28-47 are provisionally rejected on the ground of obviousness-type double patenting over claims 1-15, 17-20 and 22-41 of Application No.

10/683,154. The '154 application has been abandoned as of July 11, 2007. Therefore, the provisional double patenting rejection should be withdrawn.

III. Rejection of Claims under 35 U.S.C. § 103(a)

A. Krause and Radhakrishnan

Claims 1-5, 7, 9-14, 18-21, 28-41 and 43-47 are rejected under 35 U.S.C. § 103(a) for alleged obviousness over Krause and U.S. Patent No. 5,049,389 to Radhakrishnan ("Radhakrishnan"). Applicants respectfully traverse the rejection.

Radhakrishnan is cited for the alleged teaching of the combination of other anti-inflammatory drugs. Nevertheless, neither Krause nor Radhakrishnan meets the claim limitations of (a) an effective average particle size of less than about 2000 nm, and (b) at least one surface stabilizer adsorbed on the surface of the active agent particles.

1. Neither Krause nor Radhakrishnan disclose the claimed effective average particle size of triamcinolone

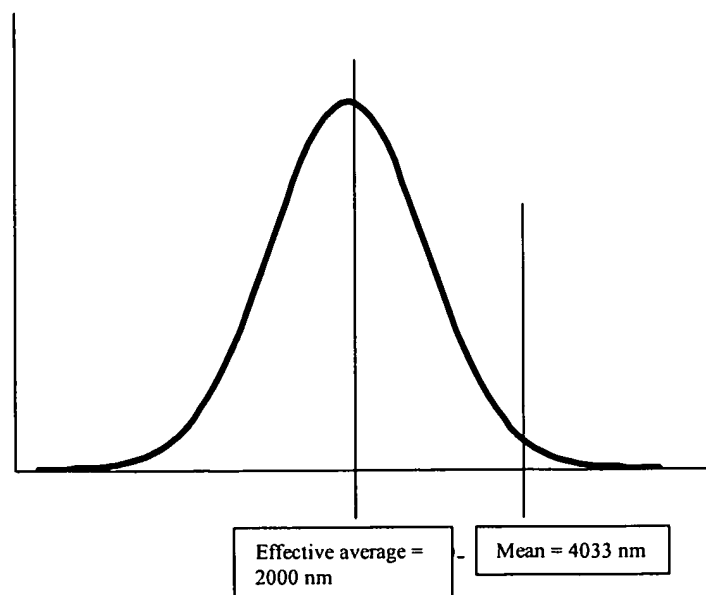
In relation to the particle size, the Examiner contends that triamcinolone acetone particles in the PLA particles would necessarily have a particle size of less than 1 micron, because the PLA particles have a mean diameter below 1 micron. This assertion by the Examiner is contradictory to his acknowledgement that, in Krause, "the loading of triamcinolone acetone entails both encapsulation and adsorption of PLA onto triamcinolone acetone." Krause describes two possibilities as to where the triamcinolone is located: inside the PLA particle (encapsulation) or on the exterior surface of the PLA particle (adsorption).

Regarding adsorption of the triamcinolone, Krause is silent as to the size of the triamcinolone when it is adsorbed on the surface of the PLA particle. Thus, a person having ordinary skills in the art could not draw any conclusion there from as to the size of the

triamcinolone. The triamcinolone adsorbed on the PLA particles therefore do not meet the size limitations of the instant claims.

Regarding the triamcinolone encapsulated within the PLA, Krause merely illustrates this event pictorially. There is nothing in Krause that identifies with any specificity that the triamcinolone itself, not the PLA particles are of any specific size, let alone disclose to a PHOSITA that the sum total of all the triamcinolone that are encapsulated have the specific effective average particle size as claimed. For example, as defined in the specification, “an effective average particle size of less than about 2000 nm” means that “at least 50% of the nanoparticulate triamcinolone and/or triamcinolone derivative particles have a weight average particle size of less than about 2000 nm” (page 54, paragraph [0158]). As such, “an effective average particle size of less than about 2000 nm” is represented by a bell-shaped curve with a peak of particle size around 2000 nm. For example, with particle sizes of 100 nm, 2000 nm and 10 microns, an effective average particle size is 2000 nm. In contrast, an arithmetic mean value is obtained by summing up a set of values, e.g., particle sizes, and dividing by the number of values. See *Stedman's* dictionary definition. For example, with particle size of 100 nm, 2000 nm and 10 microns, the mean particle size is 4033 nm.

The definitions of particle sizes are further illustrated in the graph below:



Therefore, the disclosure in Krause of PLA encapsulated triamcinolone particles having a mean diameter of less than 1 micron, does not disclose or fairly suggest to one skilled in the art the element of the claims that require the composition to comprise particles of triamcinolone having an effective average particle size of less than 2000 nm.

2. Krause use of PLA does not teach or suggest the claimed surface stabilizer

Concerning the surface stabilizer, the Examiner's assertion that the PLA reads on the surface stabilizers of the invention contradicts with her own interpretation of the cited art. The Examiner acknowledges that "the PLA necessarily stabilize[s] the triamcinolone particles as PLA affected the drug release and tissue distribution thereby stabilizing the drug in human system" (final Office Action, page 4, lines 2-4 from the bottom). The surface stabilizers of the present invention are substances adsorbed to the surface of the triamcinolone particles to maintain the small particle size of the drug particles and prevent aggregation of the particles. In the human system, the size of the drug particles of the present invention allows for increase dissolution of the drug, as opposed to Krause which teaches stabilization of the drug.

In view of the foregoing, Krause and Radhakrishnan, either alone or in combination, fail to render the claimed invention obvious because they do not teach or suggest all of Applicants' claim limitations.

Furthermore, the Examiner asserts that "Krause et al. also teaches...the inclusion of gelatin solution (i.e. **additional stabilizer**, instant claims 11-14) at 0.5% w/w" (final Office Action, page 6, lines 16-18; emphasis added). It is unclear how this teaching renders the claims at issue obvious. In particular, claim 14, which ultimately depends from claim 1, does not recite an "additional surface stabilizer", but rather further defines the surface stabilizer of claim 1. Claim 14 does not recite PLA, and Krause does not recite any of the surface stabilizers recited in claim 14. Applicants note that gelatin is listed as a surface stabilizer of Claim 14. There is no

disclosure in Krause, however, that would lead a person having ordinary skills in the art to understand that the gelatin mentioned in Krause is acting as a surface stabilizer which is adsorbed on the surface of the triamcinolone particles. In fact, gelatin could not be adsorbed on the surface of the triamcinolone particles, particularly in the case where Krause teaches that the triamcinolone is encapsulated by the PLA. Accordingly, the Examiner fails to advance any valid basis in support of the rejection of claim 14.

B. Krause, Radhakrishnan and Unger

Claims 6, 17 and 22 are rejected under 35 U.S.C. § 103(a) for alleged obviousness over Krause in view of Radhakishnan, and further in view of U.S. Patent No. 5,542,935 to Unger et al. (“Unger”). Applicants respectfully traverse the rejection.

Claims 6, 17 and 22 all depend from claim 1, which is non-obvious over Krause and Radhakishnan pursuant to the discussions above. Unger is cited for the alleged teaching of topical administration of encapsulated therapeutic drugs but fails to remedy the deficiencies of Krause and Radhakishnan.

Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is warranted.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit

card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Nov 20, 2008

By Michele M. Simkin

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717